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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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CROWELL & MORING LLP INTELLECTUAL PROPERTY GROUP P.O. BOX 14300 WASHINGTON, DC 20044-4300			EXAMINER WHITEMAN, BRIAN A	
			ART UNIT 1635	PAPER NUMBER
DATE MAILED: 02/23/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/818,943

Applicant(s)

ERIKSSON ET AL.

Examiner

Brian Whiteman

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-9,12,14,15,18,19,20,22,23,24,25,29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-9,12,14,15,18-20,22-25 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Non-Final Rejection

Claims 1, 5-9, 12, 14, 15, 18, 19, 20, 22, 23, 24, 25, and 29 are pending examination.

Applicant's traversal, the amendment to claims 1, 5, 12, 18, 19, 20, 22, 23, 24, and 25, and the addition of claim 29, the cancellation of claims 2-4, 10, 11, 13, 16, 17, 21, and 26-28 filed on 11/25/03 is acknowledged and considered.

Claim Objections

Claims 15, 20, 22, 23, 24, 25, 26, 27, and 28 remain objected to because of the following informalities: the phrases "A method according to claim" and "a transgenic mouse according to claim" are improper dependent phrases for the dependent claims. Suggest replacing the first term of each phrase with -- The --. Appropriate correction is required.

Applicant's arguments, filed 11/25/03, with respect to claim objection have been fully considered and are not persuasive. The objection of claims 15, 20, 22, 23, 24, 25, 26, 27, and 28 has not been withdrawn because other than asserting that the objection is improper, the applicants provide no reasons for why the objection is improper. The objection remains because the claims have improper dependent phrases. For example, claim 15 depends on claim 9, and claim 9 recites, "the mouse" (one mouse) and does not recite mice. However, claim 15 recites, "a mouse," indicating that there are mice in claim 9 and there is only one mouse in claim 9.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-9, 12, 14, 15, 18-20, 22-25, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse whose genome comprises a transgenic DNA encoding a polynucleotide sequence operably linked to an alpha myosin heavy chain promoter, wherein the polynucleotide sequence encodes a polypeptide comprising the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 2, wherein the transgenic mouse over-expresses the polypeptide and develops myocytes hypertrophy or heart fibrosis, wherein the mouse is heterozygous for the transgenic DNA, does not reasonably provide enablement for making and using a transgenic mouse whose genome comprises a transgenic DNA encoding a polynucleotide sequence operably linked to a suitable heart-specific promoter, wherein the polynucleotide sequence encodes a polypeptide comprising the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 2 that over-expresses a polypeptide having a PDGF-C and develops myocytes hypertrophy or heart fibrosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention is directed to making and using a transgenic mouse whose genome comprises a transgenic DNA encoding a polynucleotide sequence operably linked to a suitable heart-specific promoter, wherein the polynucleotide sequence encodes a polypeptide comprising the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 2 that over-expresses a polypeptide having a PDGF-C and develops myocytes hypertrophy or heart fibrosis. The field of the invention is directed to producing a transgenic mouse with a desired phenotype.

The art of record teaches that the art of transgenic is not predictable art with respect to transgene behavior and the resulting phenotype. While the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic mouse comprising a transgenic DNA encoding PDGF-C; it is not predictable if the transgene would be expressed at a level and specificity sufficient to cause a particular phenotype. For example, the level and specificity of expression of a transgene (e.g. PDGF-C) as well as the resulting phenotype of the transgenic mouse are directly dependent on the specific transgene construct. The individual gene of interest, coding, or non-coding sequences present in the transgene construct, the specificity of transgene integration into the genome, for example, are all important factors in controlling the expression of a transgene in the production of genetically modified animals, which exhibit a particular phenotype. This observation is supported by Wall (Theriogenology, 1996) who states "Our understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior." See page 61, last paragraph. See also Houdebine (Journal of Biotechnology, 1997) who discloses that in the field of transgenics, constructs must be designed case by case without general rules to obtain good expression of a transgene (page 275, column 1, 1st paragraph); e.g. specific promoters, presence or absence of introns, etc. With regard to the

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importance of promoter selection, Niemann states that the transgenic pigs made with different promoters regulating expression of a growth hormone gene give disparate phenotypes- one deleterious to the pig, the other compatible with pig health (Transg. Res., 7:73, 1997).

Furthermore, Sigmund teaches that the random nature of transgene insertion, resulting founder mice can contain the transgene at a different chromosomal site, and that the position of the transgene effects expression, and thus the observed phenotype (Arterosc. Throm. Vasc. Biol. 20: 1426, 2000, cited on PTO-892 mailed 12/20/01).

The specification recites that the invention features a genus of transgenic non-human mammals, which over-expresses PDGF-C and goes on to contemplate that there are two techniques for producing the transgenic non-human mammals (page 9, lines 25-31). The specification cites prior art pertaining to methods for generating transgenic mice using fertilized eggs and pro-nuclei injection (page 20). In addition, the as-filed specification provides the second method for producing transgenic mice, which involves modification of embryonic stem cells using transgenic DNA (pages 21-23). The specification produces a transgenic mouse whose genome comprises a transgenic DNA encoding a polynucleotide sequence operably linked to an alpha myosin heavy chain promoter, wherein the polynucleotide sequence encodes a polypeptide comprising the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 2, wherein the transgenic mouse over-expresses the polypeptide and develops myocytes hypertrophy or heart fibrosis, wherein the mouse is heterozygous for the transgenic DNA. The specification does not produce a homozygous mouse with the transgenic DNA with a phenotype. The specification contemplates that the transgenic mice can be used in a method for identifying PDGF-C

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antagonist, compounds that inhibit hypertrophy, and compounds that inhibit cardiac fibrosis (pages 30-31).

The claims embrace making and using a transgenic mouse whose genome comprises a transgenic DNA encoding a polynucleotide sequence operably linked to a suitable heart specific promoter, wherein the polynucleotide sequence encodes a polypeptide comprising the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 2, wherein the transgenic mouse over-expresses the polypeptide and develops myocytes hypertrophy or heart fibrosis. The claims embrace making and using a mouse that is homozygous or heterozygous for the transgenic DNA. The claimed invention is enabled for a transgenic mouse whose genome comprises a transgenic DNA encoding a polynucleotide sequence operably linked to an alpha myosin heavy chain promoter, wherein the polynucleotide sequence encodes a polypeptide comprising the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 2, wherein the transgenic mouse over-expresses the polypeptide and develops myocytes hypertrophy or heart fibrosis, wherein the mouse is heterozygous for the transgenic DNA. However, in view of the In Re Wands Factors, the claimed invention is not enabled for full scope of the claimed invention. The specification does not teach one skilled in the art how to make and use the full scope of the claimed invention. The specification recites using an alpha myosin heavy chain promoter for producing the claimed transgenic mouse. However, the alpha myosin heavy chain promoter is not a heart specific promoter. The specification does not teach one skilled in the art how to use a suitable heart specific promoter in the transgenic DNA for producing the claimed transgenic mouse. The art of record teaches that the alpha myosin heavy chain promoter can be used to express a transgene in a different organ. See Subramaniam et al., The Journal of Biological Chemistry, 266: 24613-24620, 1991. The

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art of record teaches that individual gene of interest, coding, or non-coding sequences present in the transgene construct, the specificity of transgene integration into the genome, for example, are all important factors in controlling the expression of a transgene in the production of genetically modified animals, which exhibit a particular phenotype. Constructs must be designed case by case. In addition, the specification does not teach a phenotype for the claimed homozygous transgenic mouse. The art of record teaches that producing a particular phenotype in a transgenic mouse is considered unpredictable. In view of the heterozygous transgenic mouse having myocytes hypertrophy or heart fibrosis, the homozygous mouse could have a lethal phenotype. The specification does not provide sufficient guidance and/or factual evidence for one skilled in the art to reasonably conclude that the homozygous mouse would not have a lethal phenotype due to the higher gene dosage of the transgene. In view of the In Re Wands Factors, the specification does not provide sufficient guidance and/or factual evidence for one skilled in art to reasonably correlate from the transgenic mouse produced in the specification to making and using the full scope of the claimed invention.

Given that specific phenotype alterations cannot be predictably achieved merely transferring a gene of interest into a mouse, specific guidance must be provided to enable the instant invention. The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. The claims embrace the making and using the claimed transgenic mouse wherein the mouse is heterozygous or homozygous with regard to the transgenic DNA, but the specification does not enable one skilled in the art to make and use the transgenic mouse wherein the mouse is homozygous with regard to the transgenic DNA. The specification does not provide sufficient guidance, and it fails to

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feature any reasonable correlation between producing the mouse in the specification to producing the claimed transgenic mouse, and, thus, a specific resulting phenotype other than the mouse taught in the specification.

In conclusion, in view of the quantity of experimentation necessary, the art of record for making a transgenic mouse over-expressing a polypeptide, the lack of direction or sufficient guidance provided by the as-filed specification for the production of the claimed transgenic mouse, the claimed invention is only enabled for a transgenic mouse whose genome comprises a transgenic DNA encoding a polynucleotide sequence operably linked to an alpha myosin heavy chain promoter, wherein the polynucleotide sequence encodes a polypeptide comprising the amino acid sequence SEQ ID NO: 1 or SEQ ID NO: 2, wherein the transgenic mouse over-expresses the polypeptide and develops myocytes hypertrophy or heart fibrosis, wherein the mouse is heterozygous for the transgenic DNA. Furthermore, the working examples for the demonstration or the reasonable correlation to the production of a transgenic mouse other than the mouse taught in the specification, in particular when the expression of the PDGF-C must occur at a level resulting in a corresponding phenotype, the unpredictable state of the art with respect to the transgene behavior in transgenic mouse, and the breadth of the claims drawn to the claimed transgenic mouse, it would require an undue amount of experimentation for one skilled in the art to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

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Claim 22, 23, and 24 remain and claims 5, 12, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite because the alpha myosin heavy chain promoter is not considered a heart specific promoter because the promoter can be used to express a transgene in another organ, e.g., lung. See Subramaniam et al., The Journal of Biological Chemistry, 266: 24613-24620, 1991. Thus, the metes and bounds of the claim are not defined with respect to the promoter.

The term "A transgenic mouse" in claim 12 is a relative term, which renders the claim indefinite. The term "A transgenic mouse" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the term are not defined by the claim. The term can refer to a wild type mouse produced by the method of claim 1 with another transgenic DNA.

Claim 20 recites the limitation "the PDGF-C biological". There is insufficient antecedent basis for this limitation in the claim. Suggest amending the limitation to read -- the PDGF-C biological activity --.

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Claim 22 remains rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: how assaying an effect of said compound on said cell in vitro and identifying the compound as a PDGF-C antagonist where the PDGF-C biological activity of said cell is altered are connected.

Applicant's arguments, filed 11/25/03, with respect to 112 second paragraph have been fully considered and are not persuasive. The rejection of claim 22 has not been withdrawn because the applicant did not argue how the amendment overcomes the rejection and the claim still does not define the omitted structural relationship.

Claim 23 remains rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: what type of control transgenic mouse is used in the method.

Suggest identifying the control as the mouse of claim 9.

Applicant's arguments, filed 11/25/03, with respect to 112 second paragraph have been fully considered and are not persuasive. The rejection of claim 23 has not been withdrawn because the applicant did not argue how the amendment overcomes the rejection and the claim still does not define the omitted element.

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Claim 24 remains rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: what type of non-treated control transgenic mouse is used in the method.

Suggest identifying the control as the mouse of claim 9.

Applicant's arguments, filed 11/25/03, with respect to 112 second paragraph have been fully considered and are not persuasive. The rejection of claim 24 has not been withdrawn because the applicant did not argue how the amendment overcomes the rejection and the claim still does not define the omitted element.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 12 is rejected under 35 U.S.C. 102(e) as being anticipated by Galvin et al., (US 6,359,194). Galvin teaches producing a homozygous transgenic mouse whose germ cells comprise a mutated rchd534-LacZ gene which lacks the MH2 domain encoding region, wherein the endogenous wild-type rchd534 gene of said mouse has been replaced with said mutated rchd534-LacZ gene which lacks the MH2 domain encoding region, and wherein said mouse displays a cardiovascular disease symptom (column 129).

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The claim reads on a mouse with a transgenic DNA comprising any exogenous polynucleotide sequence. The mouse could be a descendent from a wild-type mouse produced by the method of claim 9 because if you backcross the mouse produced by the method according to claim 9 with a non-transgenic mouse, the litter would comprise a wild-type mouse. The wild-type mouse could then be used for producing the transgenic mouse taught by Galvin.

Suggest inserting the phenotype limitation from claim 1 in claim 12 to overcome the 102(e) rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al., (US Patent 6,432,673) taken with Wagner et al., (US 6,492,575).

Gao teaches using a nucleotide sequence that encodes a murine zveg3 amino acid sequence (SEQ ID NO: 43) that is 100% identical to the claimed murine amino acid sequence set forth in SEQ ID NO: 2 column 6). Gao teaches making transgenic mice that over-express zveg3 (columns 49-52). Gao teaches that mice had enlargement of the liver and spleen (column 52). Gao further teaches that transgenic mice that over-express zveg3 under a tissue specific promoter or tissue-restricted promoter can be used to determine whether or not over-expression caused a phenotypic change (column 36, line 64-column 37, line 15). Gao teaches injecting plasmid DNA into fertilized eggs and injecting the eggs into pseudopregnant recipients (column 50). Gao further teaches that a DNA sequence encoding a zveg3 polypeptide is operably linked to other genetic elements required for its expression, generally including a transcription promoter and terminator, within an expression vector. However, Gao does not specifically teach using mouse embryonic stem cells to produce the transgenic mouse.

However, at the time the invention was made, Wagner teaches a method of producing a transgenic mouse with a desired phenotype using mouse embryonic stem cells (columns 3 and 15). Using this method compared to conventional methods of producing transgenic mouse, the method provides a more effective, rapid and economical method of producing mutant mice fetuses (column 4).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the inventions was made to combine the work of Gao taken with the method taught by Wagner to produce the transgenic mouse taught by Gao. One of ordinary skill in the art would have been motivated to use the method taught by Wagner to produce the transgenic mouse because Wagner

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teaches that this method compared to conventional methods of producing transgenic mouse is a more effective, rapid and economical method.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments, filed 11/25/03, with respect to claim objection have been fully considered and are persuasive. The objection of claim 18, 19 and 25 has been withdrawn because of the amendment to the claims.

Applicant's arguments, filed 11/25/03, with respect to claim objection have been fully considered and are persuasive. The objection of claim 23 and 24 has been withdrawn because of the amendment to the claims.

Applicant's arguments, filed 11/25/03, with respect to claim objection have been fully considered and are persuasive. The objection of claim 28 has been withdrawn because of cancellation of the claim.

Applicant's arguments, filed 11/25/03, with respect to 112 second paragraph have been fully considered and are persuasive. The objection of claims 1, 5, 6, 7, 8, 9, 12, 14, 15, 20, 22, 23, 24, 25, 26, 27, and 28 has been withdrawn because of cancellation of the claims 26-28 and the amendment to the independent claims.

Applicant's arguments, filed 11/25/03, with respect to the rejection(s) of claim 20 under 112 second paragraph have been fully considered and are persuasive. Therefore, the rejection of claim 20 has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the lack of antecedent basis for the term "PDGF-C biological".

Applicant's arguments, filed 11/25/03, with respect to the rejection(s) of claim 12 under 102(b) over Paigen et al. have been fully considered and are persuasive. Therefore, the rejection of claim 12 has been withdrawn because of the amendment to the claim. See page 8. However, upon further consideration, a new ground(s) of rejection is made in view of amendment to claim 12.

Applicant's arguments, filed 11/25/03, with respect to the rejection(s) under 102(e) over Gao et al., have been fully considered and are persuasive. Therefore, the rejection of Claims 1, 8, 9, 12, 14, 15, 18, 19, 20, 22, 23, 24, 25, 26, 27, and 28 has been withdrawn because of the amendment to the independent claims to recite the phenotype, "wherein the transgenic mouse develops myocytes hypertrophy or heart fibrosis." See page 8. The phenotype is not taught by the prior art.

Applicant's arguments, filed 11/25/03, with respect to rejection under 103(a) over Gao et al., taken with Prusiner et al., have been fully considered and are persuasive. The rejection of Claims 1, 6, and 7 has been withdrawn because of the amendment to the independent claims.

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See page 8. However, upon further consideration, a new ground(s) of rejection is made in view of addition of claim 29.

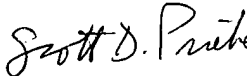
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635


SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER